

CLAIMSWHAT WE CLAIM IS:

1. An isolated monoclonal antibody having an isotype that fixes  
5 complement and a variable region that binds to the epitope on CD147 bound by the IgM monoclonal antibody ABX-CBL, with the proviso that the antibody is not CBL1.

2. The antibody of Claim 1, wherein the antibody in the presence of complement acts to selectively kill cells selected from the group consisting of activated T-cells, activated B-cells, and monocytes but is substantially non-toxic to  
10 resting T-cells and resting B-cells.

3. The antibody of Claim 1, wherein the antibody is a human antibody.

4. The antibody of Claim 1, wherein the isotype is selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3.

5. The antibody of Claim 2, wherein the antibody is a human antibody.

6. The antibody of Claim 2, wherein the isotype is selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3.

7. An isolated monoclonal antibody having an isotype that fixes  
20 complement and a variable region that binds to CD147 on populations of activated T-cells, activated B-cells, and resting or activated monocytes, that, in the presence of complement, selectively depletes such populations through complement mediated killing while being substantially nontoxic to other cells, with the proviso that the antibody is not CBL1.

8. The antibody of Claim 7, wherein the antibody is a human antibody.

9. The antibody of Claim 7, wherein the isotype is selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3.

10. An isolated monoclonal antibody having the following characteristics:

- 30 (a) binds to CD147;  
(b) shows a binding against CEM cell lysates on Western blot similar to that provided in Figure 1;

- (c) an isotype selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3;
- (d) competes with ABX-CBL for binding to CD147;
- (e) cross reacts with hn-RNP-k protein;
- (f) binds to a consensus sequence on CD147 comprising RVRSS;
- (g) selectively kills activated T-cells, activated B-cells, and monocytes in a MLR assay only in the presence of complement; and
- (h) is substantially non-toxic to cells expressing CD55 and CD59, with and without the presence of complement,

with the proviso that the antibody is not CBL1.

11. A method to select an anti-CD147 antibodies for the treatment of disease, comprising:

generating antibodies that bind to CD147 and that are capable of binding complement;

assaying the antibodies for one or more of the following properties:

- (a) competition with ABX-CBL for binding to CD147;
  - (b) capability to selectively kill activated T-cells, activated B-cells, and monocytes in a MLR assay only in the presence of complement; and
  - (c) being substantially non-toxic to cells expressing CD55 and CD59, with and without the presence of complement,
- with the proviso that the antibody is not CBL1.

- 12. The method of Claim 11, further comprising the following property:
  - (d) binding to CEM cell lysates on Western blot in a manner similar to that provided in Figure 1.
- 13. The method of Claim 11, further comprising the following property:
  - (e) binding to a consensus sequence in a peptide of RXRS.
- 14. The method of Claim 11, further comprising the following property:
  - (f) cross reacts with hn-RNP-k protein.
- 15. The method of Claim 11, further comprising the following property:

(g) binding to a form of CD147 expressed by COS cells and *E. coli* cells.

16. A method to treat disease, comprising providing an antibody that has an isotype that fixes complement and a variable region that binds to CD147 on populations of activated T-cells, activated B-cells, and resting or activated monocytes, that, in the presence of complement, selectively depletes such populations through complement mediated killing while being substantially nontoxic to other cells, with the proviso that the antibody is not CBL1.

17. The method of Claim 16, wherein the antibody is a human antibody.

18. The method of Claim 16, wherein the isotype is selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3.

19. A method to treat GVHD, comprising providing an antibody that has an isotype that fixes complement and a variable region that binds to CD147 on populations of activated T-cells, activated B-cells, and resting or activated monocytes, that, in the presence of complement, selectively depletes such populations through complement mediated killing while being substantially nontoxic to other cells, with the proviso that the antibody is not CBL1.

20. The method of Claim 19, wherein the antibody is a human antibody.

21. The method of Claim 19, wherein the isotype is selected from the group consisting of murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3.

22. A monoclonal antibody that binds to an epitope on CD147 comprising the consensus sequence RVRSH, wherein the antibody is not CBL1.

23. The antibody of Claim 22, wherein the antibody is a human antibody.

24. An isolated peptide comprising the sequence selected from the group consisting of RXRS, RXRSH, RVRS, and RVRSH.

25. Use of the peptide of Claim 24 for the generation of antibodies.

26. A human monoclonal antibody that binds to CD147.

27. A kit for the treatment of diseases having an etiology characterized by a harmful presence of activated T cells, B cells, or monocytes, comprising:

(a) a liquid preparation comprising an amount of an anti-CD147 antibody in a pharmaceutically acceptable carrier and

(b) instructions on administering said preparation to a patient suffering from a disease having the etiology characterized by a harmful presence of activated T cells, B cells, or monocytes to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody.

28. The kit of Claim 27, wherein the antibody comprises ABX-CBL.

29. The kit of Claim 27, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

30. The kit of Claim 27, wherein the disease comprises GVHD.

31. An article of manufacture for use in the treatment of diseases having an etiology characterized by a harmful presence of activated T cells, B cells, or monocytes, comprising:

(a) a sterile vial;

(b) an anti-CD147 monoclonal antibody in a pharmaceutically acceptable carrier contained within the vial; and

(c) instructions for administration of the antibody to a patient suffering from such a disease in a manner to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

32. The article of Claim 31, wherein the antibody comprises ABX-CBL.

33. The article of Claim 31, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

34. The kit of Claim 31, wherein the disease comprises GVHD.

35. A kit for the treatment of diseases having an etiology characterized by  
5 a harmful presence of activated T cells, B cells, or monocytes, comprising:  
(a) a liquid preparation comprising an amount of an anti-CD147  
antibody designated ABX-CBL in a pharmaceutically acceptable carrier and  
(b) instructions on administering said preparation to a patient suffering  
from a disease having the etiology characterized by a harmful presence of  
10 activated T cells, B cells, or monocytes in a series of administrations to  
provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of  
the antibody in each administration.

36. The kit of Claim 35, wherein the instructions further include  
15 instructions for the administration of the antibody in a series of administrations to  
provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the  
antibody in each administration.

37. The kit of Claim 35, wherein the disease comprises GVHD.

38. An article of manufacture for use in the treatment of diseases having an  
etiology characterized by a harmful presence of activated T cells, B cells, or  
monocytes, comprising:

- (a) a sterile vial;  
25 (b) an anti-CD147 monoclonal antibody designated ABX-CBL in a  
pharmaceutically acceptable carrier contained within the vial; and  
(c) instructions for administration of the antibody to a patient suffering  
from such a disease in a manner to provide a dosage in the range of from about  
0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

39. The article of Claim 38, wherein the instructions further include  
instructions for the administration of the antibody in a series of administrations to

provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

40. The article of Claim 38, wherein the disease comprises GVHD.

41. A kit for the treatment GVHD, comprising:

(a) a liquid preparation comprising an amount of an anti-CD147 antibody in a pharmaceutically acceptable carrier and

(b) instructions on administering said preparation to a patient suffering from GVHD in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

42. The kit of Claim 41, wherein the antibody comprises ABX-CBL.

43. The kit of Claim 41, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

44. An article of manufacture for use in the treatment of GVHD, comprising:

(a) a sterile vial;

(b) an anti-CD147 monoclonal antibody in a pharmaceutically acceptable carrier contained within the vial; and

(c) instructions for administration of the antibody to a patient suffering from GVHD in a manner to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

45. The article of Claim 44, wherein the antibody comprises ABX-CBL.

46. The article of Claim 44, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

47. A kit for the treatment of GVHD, comprising:

(a) a liquid preparation comprising an amount of an anti-CD147 antibody designated ABX-CBL in a pharmaceutically acceptable carrier and

(b) instructions on administering said preparation to a patient suffering from GVHD in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

48. The kit of Claim 47, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

49. An article of manufacture for use in the treatment of GVHD, comprising:

(a) a sterile vial;

(b) an anti-CD147 monoclonal antibody designated ABX-CBL in a pharmaceutically acceptable carrier contained within the vial; and

(c) instructions for administration of the antibody to a patient suffering from GVHD in a manner to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

50. The article of Claim 49, wherein the instructions further include instructions for the administration of the antibody in a series of administrations to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

51. A pharmaceutical composition, comprising an anti-CD147 monoclonal antibody designated ABX-CBL in a pharmaceutically acceptable diluent, buffer, or excipient.

5 52. The pharmaceutical composition of Claim 51, wherein the antibody is provided in a dosage from about 0.1 mg/kg and about 0.2 mg/kg.

53. A method for the treatment of diseases having an etiology characterized by a harmful presence of activated T cells, B cells, or monocytes, comprising administering a liquid preparation comprising an amount of an anti-CD147 antibody in a pharmaceutically acceptable carrier to a patient suffering from such disease.

54. The method of Claim 53, wherein the antibody comprises ABX-CBL.

55. The method of Claim 53, wherein the administration is conducted to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.

56. The method of Claim 53, wherein the disease comprises GVHD.

57. A method for the treatment of GVHD comprising administering a liquid preparation comprising an amount of an anti-CD147 antibody in a pharmaceutically acceptable carrier to a patient suffering from GVHD.

58. The method of Claim 57, wherein the antibody comprises ABX-CBL.

59. The method of Claim 57, wherein the administration is conducted to provide a dosage in the range of from about 0.1 mg/kg to about 0.3 mg/kg of the antibody in each administration.



60. The human antibody according to Claim 26, wherein the heavy chain has an amino acid sequence selected from the group consisting of : SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; SEQ ID NO: 29; SEQ ID NO: 31; SEQ ID NO:33; SEQ ID NO: 35; SEQ ID NO:37; SEQ ID NO: 39; SEQ ID NO: 40; and SEQ ID NO.

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61. The human antibody according to claim 26, wherein the light chain has an amino acid sequence selected from the group consisting of: SEQ ID NO: 24; SEQ ID NO: 26; SEQ ID NO: 28; SEQ ID NO: 30; SEQ ID NO: 32; SEQ ID NO: 34; SEQ ID NO:36; SEQ ID NO: 38; and SEQ ID NO: 41.

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